

MEDLEN & CARROLL, LLP
101 Howard Street, Suite 350
San Francisco, California 94105
415/904-6500



PATENT

Attorney Docket No. VACCINE-07971

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: David R. Milich *et al.*

Serial No.: 10/630,074

Group No.:

Filed: 07/30/2003

Examiner:

Entitled: **Human Hepatitis B Virus Core Proteins As
Vaccine Platforms And Methods Of Use
Thereof**

INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

CERTIFICATE OF MAILING UNDER 37 CFR § 1.8(a)

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to the: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on 10-29-2003

By: 

Cliff Cannon-Cin

Sir or Madam:

The citations listed below, copies attached, may be material to the examination of the above-identified application, and are therefore submitted in compliance with the duty of disclosure defined in 37 C.F.R. §§ 1.56 and 1.97. The Examiner is requested to make these citations of official record in this application.

The following patents are referred to in the body of the specification:

- WO 02/13765 published 12/21/02;
- U.S. Patent No. 4,683,195 issued 7/28/87 to Mullis *et al.*
- U.S. Patent No. 4,683,202 issued 7/28/87 to Mullis; and
- U.S. Patent No. 4,965,188 issued 10/23/90 to Mullis *et al.*

The following printed publications are referred to in the body of the specification:

- Pumpens and Grens (2001) "HBV Core Particles as a Carrier for B Cell/T Cell Epitopes," Intervirology 44:98-114;

- Jegerlehner *et al.* "A molecular assembly system that renders antigens of choice highly repetitive for induction of protective B cell responses," (2002) *Vaccine* 20:3104;
- Anderson and Young, Quantitative Filter Hybridization, in *Nucleic Acid Hybridization* [1985];
- Smith and Waterman (1981) "Comparison of Biosequences," *Adv. Appl. Math.* 2: 482-489;
- Needleman and Wunsch (1970) "A General Method Applicable to the Search for Similarities in the Amino Acid Sequence of Two Proteins," *J. Mol. Biol.* 48: 443-453;
- Pearson and Lipman (1988) "Improved tools for biological sequence comparison," *Proc. Natl. Acad. Sci. U.S.A.* 85:2444;
- Sambrook *et al.*, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Press, NY, pp 9.31-9.58, 1989;
- Sambrook, *et al.*, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Press, NY, pp 7.39-7.52, 1989;
- GenBank Accession No. NKVLC2 printed 7/16/99;
- GenBank Accession No. NP_040993 printed 12/8/02;
- Winter and Milstein (1991) "Man-made antibodies," *Nature* 349:293-299;
- Böttcher *et al.* (1997) "Determination of the fold of the core protein of hepatitis B virus by electron cryomicroscopy," *Nature* 386:88-91;
- Conway *et al.* (1997) "Visualization of a 4-helix bundle in the hepatitis B virus capsid by cryo-electron microscopy," *Nature* 386:91-94;
- Salfeld *et al.* (1989) "Antigenic Determinants and Functional Domains in Core Antigen and e Antigen from Hepatitis B Virus," *J Virol.* 63:798-808;
- Schodel *et al.* (1992) "The Position of Heterologous Epitopes Inserted in Hepatitis B Virus Core Particles Determines Their Immunogenicity," *J Virol.* 66:106-114;
- Milich *et al.* (1995) "The Hepatitis Nucleocapsid as a Vaccine Carrier Moiety," *Ann NY Acad Sci.* 754:187-201;

- Pumpens *et al.* (1995) "Hepatitis B Virus Core Particles as Epitope Carriers," Intervirology 38:63-74;
- Clarke *et al.* (1987) "Improved immunogenicity of a peptide epitope after fusion to hepatitis B core protein," Nature 330:381-384;
- Schodel *et al.* (1994) "Immunity to Malaria Elicited by Hybrid Hepatitis B Virus Core Particles Carrying Circumsporozoite Protein Epitopes," J Exp Med. 180:1037-1046;
- Schodel *et al.* "Immunization with Hybrid Hepatitis B Virus Core Particles Carrying Circumsporozoite Antigen Epitopes Protects Mice Against *Plasmodium yoelii* Challenge," (1997) Behring Inst Mitt. 114-119;
- Milich *et al.* (1997) "Role of B cells in antigen presentation of the hepatitis B core," Proc Natl Acad Sci USA 94:14648-14653;
- Kratz *et al.* (1999) "Native display of complete foreign protein domains on the surface of hepatitis B virus capsids," Proc Natl Acad Sci USA 96:1915-1920;
- Chen *et al.* (2000) "Nondeletional T-Cell Receptor Transgenic Mice: Model for the CD4+ T-Cell Repertoire in Chronic Hepatitis B Virus Infection," J. Virol. 74:7587-7599;
- Lazdina *et al.* (2001) "Molecular Basis for the Interaction of the Hepatitis B Virus Core Antigen with the Surface Immunoglobulin Receptor on Naive B Cells," J Virol. 75:6367-6374;
- Cao *et al.* (2001) "Hepatitis B Virus Core Antigen Binds and Activates Naive Human B Cells In Vivo: Studies with a Human PBL-NOD/SCID Mouse Model," J Virol. 75:6359-6366;
- Anttila *et al.* (1998) "Avidity of IgG for *Streptococcus pneumoniae* Type 6B and 23F Polysaccharides in Infants Primed with Pneumococcal Conjugates and Boosted with Polysaccharide or Conjugate Vaccines," J Infect Dis. 177:1614-1621;
- Arad *et al.* (2000) "Superantigen antagonist protects against lethal shock and defines a new domain for T-cell activation," Nat Med. 6:414-421;
- Visvanathan *et al.* (2001) "Inhibition of Bacterial Superantigens by Peptides and Antibodies," Infect Immunol. 69:875-884;

- DeVelasco *et al.* (1994) "Adjuvant Quil A improves protection in mice and enhances opsonic capacity of antisera induced by pneumococcal polysaccharide conjugate vaccines," Vaccine 12:1419-1422;
- Koletzki *et al.* (1997) "Mosaic hepatitis B virus core particles allow insertion of extended foreign protein segments," J Gen Virol. 78:2049-2053;
- Smiley and Minion (1993) "Enhanced readthrough of opal (UGA) stop codons and production of *Mycoplasma pneumoniae* P1 epitopes in *Escherichia coli*," Gene 134:33-40;
- GenBank Accession No. NM 009778 printed April 2003;
- Dempsey *et al.* (1996) "C3d of Complement as a Molecular Adjuvant: Bridging Innate and Acquired Immunity," Science 271:348-350;
- Tedder *et al.* (1994) "The CD19/CD21 signal transduction complex of B lymphocytes," Immunol Today 15:437-442;
- GenBank Accession No. X65453 printed April 2001;
- Morris *et al.* (1999) "Incorporation of an Isoleucine Zipper Motif Enhances the Biological Activity of Soluble CD40L (CD154)," J. Biol. Chem. 274:418-423;
- Mackay and Browning (2002) "Baff: A Fundamental Survival Factor for B Cells," Nature Reviews Immunology 2:465-475;
- GenBank Accession No. NM 008479 printed April 2003;
- El mir and Triebel (2000) "A Soluble Lymphocyte Activation Gene-3 Molecule Used as a Vaccine Adjuvant Elicits Greater Humoral and Cellular Immune Responses to Both Particulate and Soluble Antigens," J. Immunol 164:5583-5589;
- Krieg *et al.* (1995) "CpG motifs in bacterial DNA trigger direct B-cell activation," Nature 374:546-549;
- Davis *et al.* (1998) "CpG DNA is a Potent Enhancer of Specific Immunity in Mice Immunized with Recombinant Hepatitis B Surface Antigen," J. Immunol. 160:870-876;
- Fouet *et al.* (1999) "*Bacillus anthracis* surface: capsule and S-layer," J Appl Microbiol. 87:251-255;

- Paoletti *et al.* (2002) "Preclinical evaluation of group B streptococcal polysaccharide conjugate vaccines prepared with a modified diphtheria toxin and a recombinant duck hepatitis B core antigen," *Vaccine* 20:370-376;
- Wang *et al.* (2003) "Construction of designer glycoconjugate vaccines with size-specific oligosaccharide antigens and site-controlled coupling," *Vaccine* 21:1112-1117;
- Bittle *et al.* (1982) "Protection against foot-and-mouth disease by immunization with a chemically synthesized peptide predicted from the viral nucleotide sequence," *Nature* 298:30-33;
- Van Lierop *et al.* (1992) "Proliferative lymphocyte responses to foot-and-mouth disease virus and three FMDV peptides after vaccination and immunization with these peptides in cattle," *Immunol.* 75:406-413;
- Wong *et al.* (2000) "Plasmids Encoding Foot-and-Mouth Disease Virus VP1 Epitopes Elicited Immune Responses in Mice and Swine and protected Swine against Viral Infection," *Virol.* 278:27-35;
- Neirynck *et al.* (1999) "A universal influenza A vaccine based on the extracellular domain of the M2 protein," *Nat Med.* 5:1157-1163;
- Heinen *et al.* (2002) "Vaccination of pigs with a DNA construct expressing an influenza virus M2-nucleotprotein fusion protein exacerbates disease after challenge with influenza A virus," *J. Gen. Virol.* 83:1851-1859;
- Pekosz and Lamb (1999) "Cell Surface Expression of Biologically Active Influenza C Virus HEF Glycoprotein Expressed from cDNA," *J Virol.* 73:8808-8812;
- Hughey *et al.* (1995) "Effects of Antibody to the Influenza A Virus M2 Protein on M2 Surface Expression and Virus Assembly," *Virol.* 212:411-421;
- Zebedee and Lamb (1989) "Growth restriction of influenza A virus by M₂ protein antibody is genetically linked to the M₁ protein," *Proc Natl Acad Sci USA* 86:1061-1065;
- Pegram and Slamon (2000) "Biological Rationale for HER2/*neu* (*c-erbB2*) as a Target for Monoclonal Antibody Therapy," *Semin Oncol.* 27:13-19;

- Schenk *et al.* (1999) "Immunization with amyloid- β attenuates Alzheimer-disease-like pathology in the PDAPP mouse," *Nature* 400:173-177;
- Chang (2000) "The pharmacological basis of anti-IgE therapy," *Nat Biotechnol.* 18:157-162;
- Maini and Taylor (2000) "Anti-Cytokine Therapy for Rheumatoid Arthritis," *Annu Rev Med.* 51:207-229;
- Chackerian *et al.* (2001) "Conjugation of a self-antigen to papillomavirus-like particles allows for efficient induction of protective autoantibodies," *J Clin Invest.* 108:415-423;
- Chackerian *et al.* (1999) "Induction of autoantibodies to mouse CCR5 with recombinant papillomavirus particles," *Proc Natl Acad Sci USA* 96:2373-2378;
- Tall (1993) "Plasma cholesteryl ester transfer protein," *Lipid Res.* 34:1255-1274;
- Barter *et al.* (1982) "Transfers and exchanges of esterified cholesterol between plasma lipoproteins," *Biochem J.* 208:1-7;
- Whitlock *et al.* (1989) "Monoclonal Antibody Inhibition of Cholesteryl Ester Transfer Protein Activity in the Rabbit," *J Clin Invest.* 84:129-137;
- Kothari *et al.* (1997) "Inhibition of cholesterol ester transfer protein by CGS 25159 and changes in lipoproteins in hamsters," *Atherosclerosis* 128:59-66;
- Sugano and Makino (1996) "Changes in Plasma Lipoprotein Cholesterol Levels by Antisense Oligodeoxynucleotides against Cholesteryl Ester Transfer Protein in Cholesterol-fed Rabbits," *J Biol Chem.* 271:19080-19083;
- Sugano *et al.* (1998) "Effect of Antisense Oligonucleotides against Cholesteryl Ester Transfer Protein on the Development of Atherosclerosis in Cholesterol-fed Rabbits," *J. Biol. Chem.* 273:5033-5036;
- Agellon *et al.* (1991) "Reduced High Density Lipoprotein Cholesterol in Human Cholesteryl Ester Transfer Protein Transgenic Mice," *J Biol Chem.* 266:10796-10801;
- Herrera *et al.* (1999) "Spontaneous combined hyperlipidemia, coronary heart disease and decreased survival in Dahl salt-sensitive hypertensive rats

transgenic for human cholesteryl ester transfer protein," Nat Med.
5:1383-1389;

- Koizumi *et al.* (1985) "Deficiency of Serum Cholesteryl-Ester Transfer Activity in Patients with Familial Hyperalphalipoproteinaemia," Atherosclerosis 58:175-186;
- Rittershaus *et al.* (2000) "Vaccine-Induced Antibodies Inhibit CETP Activity In Vivo and Reduce Aortic Lesions in a Rabbit Model of Atherosclerosis," Arterioscler Thromb Vasc Biol. 20:2106-2112;
- Milich *et al.* (1998) "The Secreted Hepatitis B Precore Antigen Can Modulate the Immune Response to the Nucleocapsid: A Mechanism for Persistence," J. Immunol. 160:2013-2021;
- Morgan *et al.* (2000) "A β peptide vaccination prevents memory loss in an animal model of Alzheimer's disease," Nature 408:982-985;
- Smith *et al.* (2002) "Predicting the failure of amyloid- β vaccine," Lancet 359:1864-1865;
- Hock *et al.* (2002) "Generation of antibodies specific for β -amyloid by vaccination of patients with Alzheimer disease," Nat Med. 8:1270-1275;
- McLaurin *et al.* (2002) "Therapeutically effective antibodies against amyloid- β peptide target amyloid- β residues 4-10 and inhibit cytotoxicity and fibrillogenesis," Nat Med. 8:1263-1269;
- Rabjohn *et al.* (2002) "Modification of Peanut Allergen Ara h 3: Effects on IgE Binding and T Cell Stimulation," Int Arch Allergy Immunol. 128:15-23;
- Beezhold *et al.* (2001) "Mutational analysis of the IgE epitopes in the latex allergen Hev b 5," J Allergy Clin Immunol. 107:1069-1076;
- Reese *et al.* (2001) "Characterization and identification of allergen epitopes: recombinant peptide libraries and synthetic, overlapping peptides," J Chromatogr B Biomed Sci Appl. 756:157-163;
- Suphioglu *et al.* (2001) "A novel grass pollen allergen mimotope identified by phage display peptide library inhibits allergen-human IgE antibody interaction," FEBS Lett. 502:46-52;

- Focke *et al.* (2001) "Nonanaphylactic synthetic peptides derived from B cell epitopes of the major grass pollen allergen, Phl p 1, for allergy vaccination," FASEB J. 15:2042-2044;
- Karpenko, *et al.* (2000) "Insertion of foreign epitopes in HBcAg: how to make the chimeric particle assemble," Amino Acids 18:329-337;
- Casal *et al.* (1999) "Parvovirus-Like Particles as Vaccine Vectors," Methods 19:174-186;
- Sadeyen *et al.* (2003) "Insertion of a foreign sequence on capsid surface loops of human papillomavirus type 16 virus-like particles reduced their capacity to induce neutralizing antibodies and delineates a conformational neutralizing epitope," Virology 309:32-40;
- Varsani *et al.* (2003) "Chimeric Human Papillomavirus Type 16 (HPV-16) L1 Particles Presenting the Common Neutralizing Epitope for the L2 Minor Capsid Protein of HPV-6 and HPV-16," J. Virol., 77:8386-8393;
- Rose *et al.* (1993) "Expression of Human Papillomavirus Type 11 L1 Protein in Insect Cells: In Vivo and In Vitro Assembly of Viruslike Particles," J Virol. 67:1936-1944;
- Gedvilaite *et al.* (2000) "Formation of Immunogenic Virus-like Particles by Inserting Epitopes into Surface-Exposed Regions of Hamster Polyomavirus Major Capsid Protein," Virol. 20:21-35;
- Pumpens *et al.* (2002) "Evaluation of HBs, HBc, and frCP Virus-Like Particles for Expression of Human Papillomavirus 16E7 Oncoprotein Epitopes," Interviol. 45:24-32;
- Roth (2000) "The yeast Ty virus-like particles," Yeast 16:785-795;
- Wagner *et al.* (1996) "Safety and Immunogenicity of Recombinant Human Immunodeficiency Virus-Like Particles in Rodents and Rhesus Macaques," Interviol. 39:93-103;
- Baumert *et al.* (1999) "Hepatitis C Virus-like Particles Synthesized in Insect Cells as a Potential Vaccine Candidate," Gastroenterology 117:1397-1407;

- Sabara *et al.* (1991) "Assembly of Double-Shelled Rotaviruslike Particles by Simultaneous Expression of Recombinant VP6 and VP7 Proteins," J. Virol. 65:6994-6997;
- Ball *et al.* (1999) "Recombinant Norwalk Virus-like Particles given Orally to Volunteers" Phase I Study," Gastroenterology 117:40-48;
- Brown *et al.* (1991) "Assembly of Empty Capsids by Using Baculovirus Recombinants Expressing Human Parvovirus B19 Structural Proteins," J. Virol. 65:2702-2706;
- Thomsen *et al.* (1994) "Assembly of Herpes Simplex Virus (HSV) Intermediate Capsids in Insect Cells Infected with Recombinant Baculoviruses Expressing HSV Capsid Proteins," J. Virol. 68:2442-2457;
- Urakawa *et al.* (1989) "Synthesis of Immunogenic, but Non-infectious, Poliovirus Particles in Insect Cells by a Baculovirus Expression Vector," J. Gen. Virol. 70:1453-1463;
- Brown *et al.* (2002) "RNA Bacteriophage Capsid-Mediated Drug Delivery and Epitope Presentation," Intervirology 45:371-380;
- French *et al.* (1990) "Assembly of Double-Shelled, Viruslike Particles of Bluetongue Virus by the Simultaneous Expression of Four Structural Proteins," J. Virol. 64:5695-5700;
- Yamshchikov *et al.* (1995) "Assembly of SIV Virus-like Particles Containing Envelope Proteins Using a Baculovirus Expression System," Virol. 214:50-58;
- Plana-Duran *et al.* "Oral immunization of rabbits with VP60 particles confers protection against rabbit hemorrhagic disease," (1996) Arch. Virol. 141:1423-1436;
- Nikura *et al.* (2002) "Chimeric Recombinant Hepatitis E Virus-like Particles as an Oral Vaccine Vehicle Presenting Foreign Epitopes," Virol. 293:273-280;
- Yao (2003) "Enhancement of mucosal immune responses by chimeric influenza HA/SHIV virus-like particles," Res. Initiat. Treat Action 8:20-21;
- Kakker *et al.* (1999) "Bovine Leukemia Virus Gag Particle Assembly in Insect Cells: Formation of Chimeric Particles by Domain-Switched Leukemia/Lentivirus Gag Polyprotein," Virol. 265:308-318;

- Milich *et al.* (1994) "Extrathymic Expression of the Intracellular Hepatitis B Core Antigen Results in T Cell Tolerance in Transgenic Mice," J. Immunol. 152:455-466;
- Milich and McLachlan (1986) "The Nucleocapsid of Hepatitis B Virus Is Both a T-Cell-Independent and a T-Cell-Dependent Antigen," Science 234:1398-1401;
- Takashi *et al.* (1983) "Immunochemical Structure of Hepatitis B e Antigen in the Serum," J Immunol. 130:2903-2911;
- Ferrari *et al.* (1990) "Cellular Immune Response to Hepatitis B Virus-Encoded Antigens in Acute and Chronic Hepatitis B Virus Infection," J Immunol. 145:3442-3449;
- Milich *et al.* (1990) "Is a function of the secreted hepatitis B e antigen to induce immunologic tolerance *in utero*," Proc. Natl. Acad. Sci. USA 87:6599-6603; and
- Calvo-Calle *et al.* (1997) "Binding of Malaria T Cell Epitopes to DR and DQ Molecules In Vitro Correlates with Immunogenicity In Vivo," J Immunol. 159:1362-1373.

Applicants have become aware of the following printed publications which may be material to the examination of this application:

- U.S. Patent No. 6,602,705 issued 8/5/03 to Barnett *et al.*;
- U.S. Patent No. 6,406,705 issued 6/18/02 to Davis *et al.*;
- U.S. Patent No. 6,231,864 issued May 15, 2001 to Birkett;
- U.S. Patent No. 4,599,230 issued July 8, 1986 to Milich *et al.*;
- U.S. Patent No. 4,599,231 issued July 8, 1986 to Milich *et al.*;
- U.S. Patent No. 4,683,136 issued July 8, 1987 to Milich *et al.*;
- U.S. Patent No. 5,726,011 issued March 10, 1998 to Milich *et al.*;
- U.S. Patent No. 4,818,527 issued April 4, 1989 to Thornton *et al.*;
- U.S. Patent No. 4,882,145 issued November 21, 1989 to Thornton *et al.*;
- U.S. Patent No. 5,143,726 issued September 1, 1992 to Thornton *et al.*;
- WO 01/98333 A2 published 12/27/01;

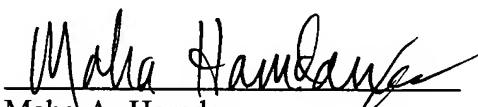
- Genbank Accession No. NP_671816 printed 8/3/93;
- Genbank Accession No. NKVLC printed 7/16/99;
- Genbank Accession No. NP_043683 printed 12/10/02;
- Heterobifunctional Cross-linkers, Pierce Chemical Technical Library;
- Milich *et al.* (2002) "Conversion of poorly immunogenic malaria repeat sequences into a highly immunogenic vaccine candidate," *Vaccine* 20:771-788;
- Wynne *et al.* (1999) "The Crystal Structure of the Human Hepatitis B Virus Capsid," *Mol. Cell.* 3:771-780;
- Hollinger and Dienstag, Chapter 82, Hepatitis B and D Viruses, in *Manual of Clinical Microbiology*, 7th ed., ASM Press, Washington, D.C., 1999
- Dubovsky, "Creating a Vaccine against Malaria," The Maralaria Vaccine Initiative, PATH (Program for Appropriate Technology in Health), January 2001;
- Falciparum Malaria MSP1 Workshop, Progress toward MSP1 Vaccine Development and Testing, The Maralaria Vaccine Initiative, PATH (Program for Appropriate Technology in Health), December 2000;
- Lu *et al.* (1999) "Immunization of Woodchucks with Plasmids Expressing Woodchuck Hepatitis Virus (WHV) Core Antigen and Surface Antigen Suppresses WHV Infection," *J. Virol.* 73:281-289;
- Menne *et al.* (1997) "Characterization of T-Cell Response to Woodchuck Hepatitis Virus Core Protein and Protection of Woodchucks from Infection by Immunization with Peptides Containing a T-Cell Epitope," *J. Virol.* 71:65-74;
- Lew *et al.* (2001) "In Vitro and In Vivo Infectivity and Pathogenicity of the Lymphoid Cell-Derived Woodchuck Hepatitis Virus," *J. Virol.* 75:1770-1782;
- Siegel *et al.* (2001) "Coadministration of Gamma Interferon with DNA Vaccine Expressing Woodchuck Hepatitis Virus (WHV) Core Antigen Enhances the Specific Immune Response and Protects against WHV Infection," *J. Virol.* 75:5036-5042;
- Birkett, U.S. Patent Application No. 09/930,915, filed Aug. 15, 2001, published July 24, 2003 as Publication No. 20030138769, and entitled "Immunogenic HBc chimeric particles having enhanced stability," and

- Brown *et al.*, U.S. patent publication No. US 20030175296 published Sept. 18, 2003, and entitled "Chimaeric hepadnavirus core antigen proteins."

This Information Disclosure Statement under 37 C.F.R. §§ 1.56 and 1.97 is not to be construed as a representation that a search has been made, that additional information material to the examination of this application does not exist, or that any one or more of these citations constitutes prior art.

Signed on behalf of:

Dated: 10-29-2003


Maha A. Hamdan
Registration No. 43,655

MEDLEN & CARROLL, LLP
101 Howard Street, Suite 305
San Francisco, California 94105
415/904-6500

FORM PTO-1449
(Modified)U.S. Department of Commerce
Patent and Trademark Office

Attorney Docket No.: VACCINE-07971

Serial No.: 10/630,074

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Include Additional Sheets If Necessary)

(37 CFR § 1.98(b))

Applicant: David R. Milich *et al.*

Filing Date: 07/30/2003

Group Art Unit:

U.S. PATENT DOCUMENTS

Examiner Initials	Cite No.	Serial / Patent Number	Issue Date	Applicant / Patentee	Class	Subclass	Filing Date
	1	4,683,195	7/28/87	Mullis <i>et al.</i>			
	2	4,683,202	7/28/87	Mullis			
	3	4,965,188	10/23/90	Mullis <i>et al.</i>			
	4	6,602,705	8/5/03	Barnett <i>et al.</i>			
	5	6,406,705	6/18/02	Davis <i>et al.</i>			
	6	6,231,864	5/15/01	Birkett			
	7	4,599,230	7/8/86	Milich <i>et al.</i>			
	8	4,599,231	7/8/86	Milich <i>et al.</i>			
	9	4,683,136	7/8/87	Milich <i>et al.</i>			
	10	5,726,011	3/10/98	Milich <i>et al.</i>			
	11	4,818,527	4/4/89	Thornton <i>et al.</i>			
	12	4,882,145	11/21/89	Thornton <i>et al.</i>			
	13	5,143,726	9/1/92	Thornton <i>et al.</i>			

FOREIGN PATENTS OR PUBLISHED FOREIGN PATENT APPLICATIONS

		Document Number	Publication Date	Country / Patent Office	Class	Subclass	Translation	
							Yes	No
	14	WO 02/13765	12/21/02 ✓	PCT				
	15	WO 01/98333 A2	12/27/01 ✓	PCT				

OTHER DOCUMENTS (Including Author, Title, Date, Relevant Pages, Place of Publication)

16 ✓	Pumpens and Grens (2001) "HBV Core Particles as a Carrier for B Cell/T Cell Epitopes," <i>Intervirology</i> 44:98-114
17 ✓	Jegerlehner <i>et al.</i> "A molecular assembly system that renders antigens of choice highly repetitive for induction of protective B cell responses," (2002) <i>Vaccine</i> 20:3104
18 ✓	Anderson and Young, Quantitative Filter Hybridization, in <i>Nucleic Acid Hybridization</i> [1985]
19 ✓	Smith and Waterman (1981) "Comparison of Biosequences," <i>Adv. Appl. Math.</i> 2: 482-489
20 ✓	Needleman and Wunsch (1970) "A General Method Applicable to the Search for Similarities in the Amino Acid Sequence of Two Proteins," <i>J. Mol. Biol.</i> 48: 443-453
21 ✓	Pearson and Lipman (1988) "Improved tools for biological sequence comparison," <i>Proc. Natl. Acad. Sci. U.S.A.</i> 85:2444
22 ✓	Sambrook <i>et al.</i> , <i>Molecular Cloning: A Laboratory Manual</i> , Cold Spring Harbor Press, NY, pp 9.31-9.58, 1989
23 ✓	Sambrook, <i>et al.</i> , <i>Molecular Cloning: A Laboratory Manual</i> , Cold Spring Harbor Press, NY, pp 7.39-7.52, 1989
24 ✓	GenBank Accession No. NKVLC2 printed 7/16/99
25 ✓	GenBank Accession No. NP_040993 printed 12/8/02

Examiner:

Date Considered:

EXAMINER:

Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449
(Modified)U.S. Department of Commerce
Patent and Trademark Office

Attorney Docket No.: VACCINE-07971

Serial No.: 10/630,074

INFORMATION DISCLOSURE STATEMENT BY APPLICANT
(Include Several Sheets If Necessary)Applicant: David R. Milich *et al.*

(37 CFR § 1.98(b))

Filing Date: 07/30/2003

Group Art Unit:

OTHER DOCUMENTS (Including Author, Title, Date, Relevant Pages, Place of Publication)

- | | | |
|----|---|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 26 | ✓ | Winter and Milstein (1991) "Man-made antibodies," Nature 349:293-299 |
| 27 | ✓ | Böttcher <i>et al.</i> (1997) "Determination of the fold of the core protein of hepatitis B virus by electron cryomicroscopy," Nature 386:88-91 |
| 28 | ✓ | Conway <i>et al.</i> (1997) "Visualization of a 4-helix bundle in the hepatitis B virus capsid by cryo-electron microscopy," Nature 386:91-94 |
| 29 | ✓ | Salfeld <i>et al.</i> (1989) "Antigenic Determinants and Functional Domains in Core Antigen and e Antigen from Hepatitis B Virus," J Virol. 63:798-808 |
| 30 | ✓ | Schodel <i>et al.</i> (1992) "The Position of Heterologous Epitopes Inserted in Hepatitis B Virus Core Particles Determines Their Immunogenicity," J Virol. 66:106-114 |
| 31 | ✓ | Milich <i>et al.</i> (1995) "The Hepatitis Nucleocapsid as a Vaccine Carrier Moiety," Ann NY Acad Sci. 754:187-201 |
| 32 | ✓ | Pumpens <i>et al.</i> (1995) "Hepatitis B Virus Core Particles as Epitope Carriers," Intervirology 38:63-74 |
| 33 | ✓ | Clarke <i>et al.</i> (1987) "Improved immunogenicity of a peptide epitope after fusion to hepatitis B core protein," Nature 330:381-384 |
| 34 | ✓ | Schodel <i>et al.</i> (1994) "Immunity to Malaria Elicited by Hybrid Hepatitis B Virus Core Particles Carrying Circumsporozoite Protein Epitopes," J Exp Med. 180:1037-1046 |
| 35 | ✓ | Schodel <i>et al.</i> "Immunization with Hybrid Hepatitis B Virus Core Particles Carrying Circumsporozoite Antigen Epitopes Protects Mice Against <i>Plasmodium yoelii</i> Challenge," (1997) Behring Inst Mitt. 114-119 |
| 36 | ✓ | Milich <i>et al.</i> (1997) "Role of B cells in antigen presentation of the hepatitis B core," Proc Natl Acad Sci USA 94:14648-14653 |
| 37 | ✓ | Kratz <i>et al.</i> (1999) "Native display of complete foreign protein domains on the surface of hepatitis B virus capsids," Proc Natl Acad Sci USA 96:1915-1920 |
| 38 | ✓ | Chen <i>et al.</i> (2000) "Nondeletional T-Cell Receptor Transgenic Mice: Model for the CD4+ T-Cell Repertoire in Chronic Hepatitis B Virus Infection," J. Virol. 74:7587-7599 |
| 39 | ✓ | Lazdina <i>et al.</i> (2001) "Molecular Basis for the Interaction of the Hepatitis B Virus Core Antigen with the Surface Immunoglobulin Receptor on Naive B Cells," J Virol. 75:6367-6374 |
| 40 | ✓ | Cao <i>et al.</i> (2001) "Hepatitis B Virus Core Antigen Binds and Activates Naive Human B Cells In Vivo: Studies with a Human PBL-NOD/SCID Mouse Model," J Virol. 75:6359-6366 |
| 41 | ✓ | Anttila <i>et al.</i> (1998) "Avidity of IgG for <i>Streptococcus pneumoniae</i> Type 6B and 23F Polysaccharides in Infants Primed with Pneumococcal Conjugates and Boosted with Polysaccharide or Conjugate Vaccines," J Infect Dis. 177:1614-1621 |
| 42 | ✓ | Arad <i>et al.</i> (2000) "Superantigen antagonist protects against lethal shock and defines a new domain for T-cell activation," Nat Med. 6:414-421 |
| 43 | ✓ | Visvanathan <i>et al.</i> (2001) "Inhibition of Bacterial Superantigens by Peptides and Antibodies," Infect Immunol. 69:875-884 |
| 44 | ✓ | DeVelasco <i>et al.</i> (1994) "Adjuvant Quil A improves protection in mice and enhances opsonic capacity of antisera induced by pneumococcal polysaccharide conjugate vaccines," Vaccine 12:1419-1422 |
| 45 | ✓ | Koletzki <i>et al.</i> (1997) "Mosaic hepatitis B virus core particles allow insertion of extended foreign protein segments," J Gen Virol. 78:2049-2053 |
| 46 | ✓ | Smiley and Minion (1993) "Enhanced readthrough of opal (UGA) stop codons and production of <i>Mycoplasma pneumoniae</i> P1 epitopes in <i>Escherichia coli</i> ," Gene 134:33-40 |
| 47 | ✓ | GenBank Accession No. NM 009778 printed April 2003 |
| 48 | ✓ | Dempsey <i>et al.</i> (1996) "C3d of Complement as a Molecular Adjuvant: Bridging Innate and Acquired Immunity," Science 271:348-350 |
| 49 | ✓ | Tedder <i>et al.</i> (1994) "The CD19/CD21 signal transduction complex of B lymphocytes," Immunol Today 15:437-442 |
| 50 | ✓ | GenBank Accession No. X65453 printed April 2001 |
| 51 | ✓ | Morris <i>et al.</i> (1999) "Incorporation of an Isoleucine Zipper Motif Enhances the Biological Activity of Soluble CD40L (CD154)," J. Biol. Chem. 274:418-423 |
| 52 | ✓ | Mackay and Browning (2002) "Baff: A Fundamental Survival Factor for B Cells," Nature Reviews Immunology 2:465-475 |
| 53 | ✓ | GenBank Accession No. NM 008479 printed April 2003 |

Examiner:

Date Considered:

EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449
(Modified)U.S. Department of Commerce
Patent and Trademark Office

Attorney Docket No.: VACCINE-07971

Serial No.: 10/630,074

INFORMATIONAL DISCLOSURE STATEMENT BY APPLICANT
(Use Several Sheets If Necessary)Applicant: David R. Milich *et al.*

(37 CFR § 1.98(b))

Filing Date: 07/30/2003

Group Art Unit:

OTHER DOCUMENTS (Including Author, Title, Date, Relevant Pages, Place of Publication)

54✓	El mir and Triebel (2000) "A Soluble Lymphocyte Activation Gene-3 Molecule Used as a Vaccine Adjuvant Elicits Greater Humoral and Cellular Immune Responses to Both Particulate and Soluble Antigens," J. Immunol 164:5583-5589
55✓	Krieg <i>et al.</i> (1995) "CpG motifs in bacterial DNA trigger direct B-cell activation," Nature 374:546-549
56✓	Davis <i>et al.</i> (1998) "CpG DNA is a Potent Enhancer of Specific Immunity in Mice Immunized with Recombinant Hepatitis B Surface Antigen," J. Immunol. 160:870-876
57✓	Fouet <i>et al.</i> (1999) " <i>Bacillus anthracis</i> surface: capsule and S-layer," J Appl Microbiol. 87:251-255
58✓	Paoletti <i>et al.</i> (2002) "Preclinical evaluation of group B streptococcal polysaccharide conjugate vaccines prepared with a modified diphtheria toxin and a recombinant duck hepatitis B core antigen," Vaccine 20:370-376
59✓	Wang <i>et al.</i> (2003) "Construction of designer glycoconjugate vaccines with size-specific oligosaccharide antigens and site-controlled coupling," Vaccine 21:1112-1117
60✓	Bittle <i>et al.</i> (1982) "Protection against foot-and-mouth disease by immunization with a chemically synthesized peptide predicted from the viral nucleotide sequence," Nature 298:30-33
61✓	Van Lierop <i>et al.</i> (1992) "Proliferative lymphocyte responses to foot-and-mouth disease virus and three FMDV peptides after vaccination and immunization with these peptides in cattle," Immunol. 75:406-413
62✓	Wong <i>et al.</i> (2000) "Plasmids Encoding Foot-and-Mouth Disease Virus VP1 Epitopes Elicited Immune Responses in Mice and Swine and protected Swine against Viral Infection," Virol. 278:27-35
63✓	Neirynck <i>et al.</i> (1999) "A universal influenza A vaccine based on the extracellular domain of the M2 protein," Nat Med. 5:1157-1163
64✓	Heinen <i>et al.</i> (2002) "Vaccination of pigs with a DNA construct expressing an influenza virus M2-nucleoprotein fusion protein exacerbates disease after challenge with influenza A virus," J. Gen. Virol. 83:1851-1859
65✓	Pekosz and Lamb (1999) "Cell Surface Expression of Biologically Active Influenza C Virus HEF Glycoprotein Expressed from cDNA," J Virol. 73:8808-8812
66✓	Hughey <i>et al.</i> (1995) "Effects of Antibody to the Influenza A Virus M2 Protein on M2 Surface Expression and Virus Assembly," Virol. 212:411-421
67✓	Zebedee and Lamb (1989) "Growth restriction of influenza A virus by M ₂ protein antibody is genetically linked to the M ₁ protein," Proc Natl Acad Sci USA 86:1061-1065
68✓	Pegram and Slamon (2000) "Biological Rationale for HER2/ <i>neu</i> (c- <i>erbB2</i>) as a Target for Monoclonal Antibody Therapy," Semin Oncol. 27:13-19
69✓	Schenk <i>et al.</i> (1999) "Immunization with amyloid- β attenuates Alzheimer-disease-like pathology in the PDAPP mouse," Nature 400:173-177
70✓	Chang (2000) "The pharmacological basis of anti-IgE therapy," Nat Biotechnol. 18:157-162
71✓	Maini and Taylor (2000) "Anti-Cytokine Therapy for Rheumatoid Arthritis," Annu Rev Med. 51:207-229
72✓	Chackerian <i>et al.</i> (2001) "Conjugation of a self-antigen to papillomavirus-like particles allows for efficient induction of protective autoantibodies," J Clin Invest. 108:415-423
73✓	Chackerian <i>et al.</i> (1999) "Induction of autoantibodies to mouse CCR5 with recombinant papillomavirus particles," Proc Natl Acad Sci USA 96:2373-2378
74✓	Tall (1993) "Plasma cholesteryl ester transfer protein," Lipid Res. 34:1255-1274
75✓	Barter <i>et al.</i> (1982) "Transfers and exchanges of esterified cholesterol between plasma lipoproteins," Biochem J. 208:1-7
76✓	Whitlock <i>et al.</i> (1989) "Monoclonal Antibody Inhibition of Cholesteryl Ester Transfer Protein Activity in the Rabbit," J Clin Invest. 84:129-137
77✓	Kothari <i>et al.</i> (1997) "Inhibition of cholesterol ester transfer protein by CGS 25159 and changes in lipoproteins in hamsters," Atherosclerosis 128:59-66

Examiner:

Date Considered:

EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449
Patent and Trademark Office

U.S. Department of Commerce

Attorney Docket No.: VACCINE-07971

Serial No.: 10/630,074

INFORMATION DISCLOSURE STATEMENT BY APPLICANT
(Use Several Sheets If Necessary)

Applicant: David R. Milich *et al.*

(37 CFR § 1.98(b))

Filing Date: 07/30/2003

Group Art Unit:

OTHER DOCUMENTS (Including Author, Title, Date, Relevant Pages, Place of Publication)

- | | |
|-------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 78 ✓ | Sugano and Makino (1996) "Changes in Plasma Lipoprotein Cholesterol Levels by Antisense Oligodeoxynucleotides against Cholesteryl Ester Transfer Protein in Cholesterol-fed Rabbits," J Biol Chem. 271:19080-19083 |
| 79 ✓ | Sugano <i>et al.</i> (1998) "Effect of Antisense Oligonucleotides against Cholesteryl Ester Transfer Protein on the Development of Atherosclerosis in Cholesterol-fed Rabbits," J. Biol. Chem. 273:5033-5036 |
| 80 ✓ | Agellon <i>et al.</i> (1991) "Reduced High Density Lipoprotein Cholesterol in Human Cholesteryl Ester Transfer Protein Transgenic Mice," J Biol Chem. 266:10796-10801 |
| 81 ✓ | Herrera <i>et al.</i> (1999) "Spontaneous combined hyperlipidemia, coronary heart disease and decreased survival in Dahl salt-sensitive hypertensive rats transgenic for human cholesteryl ester transfer protein," Nat Med. 5:1383-1389 |
| 82 ✓ | Koizumi <i>et al.</i> (1985) "Deficiency of Serum Cholesteryl-Ester Transfer Activity in Patients with Familial Hyperalphalipoproteinaemia," Atherosclerosis 58:175-186 |
| 83 ✓ | Rittershaus <i>et al.</i> (2000) "Vaccine-Induced Antibodies Inhibit CETP Activity In Vivo and Reduce Aortic Lesions in a Rabbit Model of Atherosclerosis," Arterioscler Thromb Vasc Biol. 20:2106-2112 |
| 84 ✓ | Milich <i>et al.</i> (1998) "The Secreted Hepatitis B Precore Antigen Can Modulate the Immune Response to the Nucleocapsid: A Mechanism for Persistence," J. Immunol. 160:2013-2021 |
| 85 ✓ | Morgan <i>et al.</i> (2000) "Aβ peptide vaccination prevents memory loss in an animal model of Alzheimer's disease," Nature 408:982-985 |
| 86 ✓ | Smith <i>et al.</i> (2002) "Predicting the failure of amyloid-β vaccine," Lancet 359:1864-1865 |
| 87 ✓ | Hock <i>et al.</i> (2002) "Generation of antibodies specific for β-amyloid by vaccination of patients with Alzheimer disease," Nat Med. 8:1270-1275 |
| 88 ✓ | McLaurin <i>et al.</i> (2002) "Therapeutically effective antibodies against amyloid-β peptide target amyloid-β residues 4-10 and inhibit cytotoxicity and fibrillogenesis," Nat Med. 8:1263-1269 |
| 89 ✓ | Rabjohn <i>et al.</i> (2002) "Modification of Peanut Allergen Ara h 3: Effects on IgE Binding and T Cell Stimulation," Int Arch Allergy Immunol. 128:15-23 |
| 90 ✓ | Beezhold <i>et al.</i> (2001) "Mutational analysis of the IgE epitopes in the latex allergen Hev b 5," J Allergy Clin Immunol. 107:1069-1076 |
| 91 ✓ | Reese <i>et al.</i> (2001) "Characterization and identification of allergen epitopes: recombinant peptide libraries and synthetic, overlapping peptides," J Chromatogr B Biomed Sci Appl. 756:157-163 |
| 92 ✓ | Suphioglu <i>et al.</i> (2001) "A novel grass pollen allergen mimotope identified by phage display peptide library inhibits allergen-human IgE antibody interaction," FEBS Lett. 502:46-52 |
| 93 ✓ | Focke <i>et al.</i> (2001) "Nonanaphylactic synthetic peptides derived from B cell epitopes of the major grass pollen allergen, Phl p 1, for allergy vaccination," FASEB J. 15:2042-2044 |
| 94 ✓ | Karpenko, <i>et al.</i> (2000) "Insertion of foreign epitopes in HBcAg: how to make the chimeric particle assemble," Amino Acids 18:329-337 |
| 95 ✓ | Casal <i>et al.</i> (1999) "Parvovirus-Like Particles as Vaccine Vectors," Methods 19:174-186 |
| 96 ✓ | Sadeyen <i>et al.</i> (2003) "Insertion of a foreign sequence on capsid surface loops of human papillomavirus type 16 virus-like particles reduced their capacity to induce neutralizing antibodies and delineates a conformational neutralizing epitope," Virology 309:32-40 |
| 97 ✓ | Varsani <i>et al.</i> (2003) "Chimeric Human Papillomavirus Type 16 (HPV-16) L1 Particles Presenting the Common Neutralizing Epitope for the L2 Minor Capsid Protein of HPV-6 and HPV-16," J. Virol., 77:8386-8393 |
| 98 ✓ | Rose <i>et al.</i> (1993) "Expression of Human Papillomavirus Type 11 L1 Protein in Insect Cells: In Vivo and In Vitro Assembly of Viruslike Particles," J Virol. 67:1936-1944 |
| 99 ✓ | Gedvilaite <i>et al.</i> (2000) "Formation of Immunogenic Virus-like Particles by Inserting Epitopes into Surface-Exposed Regions of Hamster Polyomavirus Major Capsid Protein," Virol. 20:21-35 |
| 100 ✓ | Pumpens <i>et al.</i> (2002) "Evaluation of HBs, HBc, and frCP Virus-Like Particles for Expression of Human Papillomavirus 16E7 Oncoprotein Epitopes," Intervirology. 45:24-32 |
| 101 ✓ | Roth (2000) "The yeast Ty virus-like particles," Yeast 16:785-795 |
| 102 ✓ | Wagner <i>et al.</i> (1996) "Safety and Immunogenicity of Recombinant Human Immunodeficiency Virus-Like Particles in Rodents and Rhesus Macaques," Intervirology. 39:93-103 |

Examiner:

Date Considered:

EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449
(Modified)U.S. Department of Commerce
Patent and Trademark Office

Attorney Docket No.: VACCINE-07971

Serial No.: 10/630,074

INFORMATION DISCLOSURE STATEMENT BY APPLICANT
(Use Several Sheets If Necessary)

(37 CFR § 1.98(b))

Applicant: David R. Milich *et al.*

Filing Date: 07/30/2003

Group Art Unit:

OTHER DOCUMENTS (Including Author, Title, Date, Relevant Pages, Place of Publication)

- | | |
|-----|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 103 | Baumert <i>et al.</i> (1999) "Hepatitis C Virus-like Particles Synthesized in Insect Cells as a Potential Vaccine Candidate," Gastroenterology 117:1397-1407 |
| 104 | Sabara <i>et al.</i> (1991) "Assembly of Double-Shelled Rotaviruslike Particles by Simultaneous Expression of Recombinant VP6 and VP7 Proteins," J. Virol. 65:6994-6997 |
| 105 | Ball <i>et al.</i> (1999) "Recombinant Norwalk Virus-like Particles given Orally to Volunteers" Phase I Study," Gastroenterology 117:40-48 |
| 106 | Brown <i>et al.</i> (1991) "Assembly of Empty Capsids by Using Baculovirus Recombinants Expressing Human Parvovirus B19 Structural Proteins," J. Virol. 65:2702-2706 |
| 107 | Thomsen <i>et al.</i> (1994) "Assembly of Herpes Simplex Virus (HSV) Intermediate Capsids in Insect Cells Infected with Recombinant Baculoviruses Expressing HSV Capsid Proteins," J. Virol. 68:2442-2457 |
| 108 | Urakawa <i>et al.</i> (1989) "Synthesis of Immunogenic, but Non-infectious, Poliovirus Particles in Insect Cells by a Baculovirus Expression Vector," J. Gen. Virol. 70:1453-1463 |
| 109 | Brown <i>et al.</i> (2002) "RNA Bacteriophage Capsid-Mediated Drug Delivery and Epitope Presentation," Intervirology 45:371-380 |
| 110 | French <i>et al.</i> (1990) "Assembly of Double-Shelled, Viruslike Particles of Bluetongue Virus by the Simultaneous Expression of Four Structural Proteins," J. Virol. 64:5695-5700 |
| 111 | Yamshchikov <i>et al.</i> (1995) "Assembly of SIV Virus-like Particles Containing Envelope Proteins Using a Baculovirus Expression System," Virol. 214:50-58 |
| 112 | Plana-Duran <i>et al.</i> "Oral immunization of rabbits with VP60 particles confers protection against rabbit hemorrhagic disease," (1996) Arch. Virol. 141:1423-1436 |
| 113 | Nikura <i>et al.</i> (2002) "Chimeric Recombinant Hepatitis E Virus-like Particles as an Oral Vaccine Vehicle Presenting Foreign Epitopes," Virol. 293:273-280 |
| 114 | Yao (2003) "Enhancement of mucosal immune responses by chimeric influenza HA/SHIV virus-like particles," Res. Initiat. Treat Action 8:20-21 |
| 115 | Kakker <i>et al.</i> (1999) "Bovine Leukemia Virus Gag Particle Assembly in Insect Cells: Formation of Chimeric Particles by Domain-Switched Leukemia/Lentivirus Gag Polyprotein," Virol. 265:308-318 |
| 116 | Milich <i>et al.</i> (1994) "Extrathymic Expression of the Intracellular Hepatitis B Core Antigen Results in T Cell Tolerance in Transgenic Mice," J. Immunol. 152:455-466 |
| 117 | Milich and McLachlan (1986) "The Nucleocapsid of Hepatitis B Virus Is Both a T-Cell-Independent and a T-Cell-Dependent Antigen," Science 234:1398-1401 |
| 118 | Takashi <i>et al.</i> (1983) "Immunochemical Structure of Hepatitis B e Antigen in the Serum," J Immunol. 130:2903-2911 |
| 119 | Ferrari <i>et al.</i> (1990) "Cellular Immune Response to Hepatitis B Virus-Encoded Antigens in Acute and Chronic Hepatitis B Virus Infection," J Immunol. 145:3442-3449 |
| 120 | Milich <i>et al.</i> (1990) "Is a function of the secreted hepatitis B e antigen to induce immunologic tolerance <i>in utero</i> ," Proc. Natl. Acad. Sci. USA 87:6599-6603 |
| 121 | Calvo-Calle <i>et al.</i> (1997) "Binding of Malaria T Cell Epitopes to DR and DQ Molecules In Vitro Correlates with Immunogenicity In Vivo," J Immunol. 159:1362-1373 |
| 122 | Genbank Accession No. NP_671816 printed 8/3/93 |
| 123 | Genbank Accession No. NKVLC printed 7/16/99 |
| 124 | Genbank Accession No. NP_043683 printed 12/10/02 |
| 125 | Heterobifunctional Cross-linkers, Pierce Chemical Technical Library |
| 126 | Milich <i>et al.</i> (2002) "Conversion of poorly immunogenic malaria repeat sequences into a highly immunogenic vaccine candidate," Vaccine 20:771-788 |
| 127 | Wynne <i>et al.</i> (1999) "The Crystal Structure of the Human Hepatitis B Virus Capsid," Mol. Cell. 3:771-780 |

Examiner:

Date Considered:

EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-144
(Modified)U.S. Department of Commerce
Patent and Trademark Office

Attorney Docket No.: VACCINE-07971

Serial No.: 10/630,074

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

Applicant: David R. Milich *et al.*

(37 CFR § 1.98(b))

Filing Date: 07/30/2003

Group Art Unit:

- | | |
|-----|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 128 | Hollinger and Dienstag, Chapter 82, Hepatitis B and D Viruses, in <i>Manual of Clinical Microbiology</i> , 7th ed., ASM Press, Washington, D.C., 1999 |
| 129 | Dubovsky, "Creating a Vaccine against Malaria," The Maralaria Vaccine Initiative, PATH (Program for Appropriate Technology in Health), January 2001 |
| 130 | Falci-parum Malaria MSP1 Workshop, Progress toward MSP1 Vaccine Development and Testing, The Maralaria Vaccine Initiative, PATH (Program for Appropriate Technology in Health), December 2000 |
| 131 | Lu <i>et al.</i> (1999) "Immunization of Woodchucks with Plasmids Expressing Woodchuck Hepatitis Virus (WHV) Core Antigen and Surface Antigen Suppresses WHV Infection," J. Virol. 73:281-289 |
| 132 | Menne <i>et al.</i> (1997) "Characterization of T-Cell Response to Woodchuck Hepatitis Virus Core Protein and Protection of Woodchucks from Infection by Immunization with Peptides Containing a T-Cell Epitope," J. Virol. 71:65-74 |
| 133 | Lew <i>et al.</i> (2001) "In Vitro and In Vivo Infectivity and Pathogenicity of the Lymphoid Cell-Derived Woodchuck Hepatitis Virus," J. Virol. 75:1770-1782 |
| 134 | Siegel <i>et al.</i> (2001) "Coadministration of Gamma Interferon with DNA Vaccine Expressing Woodchuck Hepatitis Virus (WHV) Core Antigen Enhances the Specific Immune Response and Protects against WHV Infection," J. Virol. 75:5036-5042 |
| 135 | Birkett, U.S. Patent Application No. 09/930,915, filed: August 15, 2001, published July 24, 2003 as Publication No. 20030138769, and entitled "Immunogenic HBc chimer particles having enhanced stability |
| 136 | Brown <i>et al.</i> , U.S. patent publication No. US 20030175296 published Sept. 18, 2003. |

Examiner:

Date Considered:

EXAMINER: Initial citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.